

**Amendments To The Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

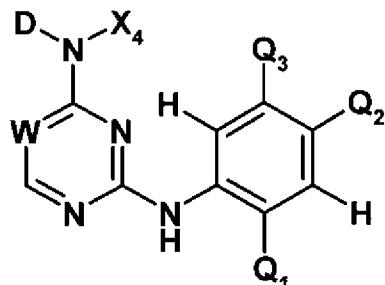
**In the Claims:**

What is claimed is:

Claims 1-12 (Cancelled)

13. (New) A method of treating cancer in a mammal, comprising: administering to said mammal

(a) a compound of formula I

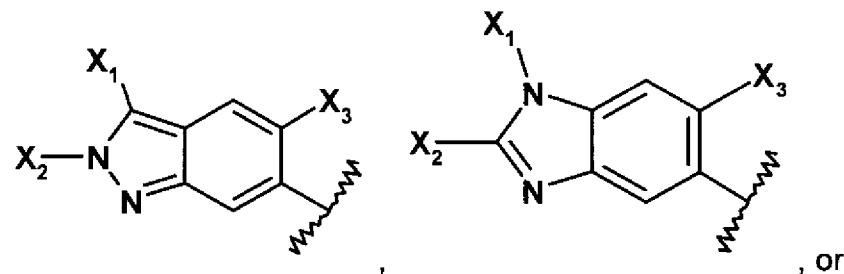


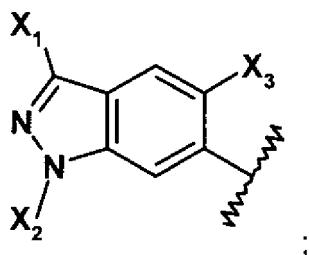
(I)

or a salt, solvate, or physiologically functional derivative thereof;

wherein:

D is





$X_1$  is hydrogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, or C<sub>1-4</sub> hydroxyalkyl;

$X_2$  is hydrogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C(O)R<sup>1</sup>, or aralkyl;

$X_3$  is hydrogen or halogen;

$X_4$  is hydrogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, heteroaralkyl, cyanoalkyl, -(CH<sub>2</sub>)<sub>p</sub>C=CH(CH<sub>2</sub>)<sub>t</sub>H, -(CH<sub>2</sub>)<sub>p</sub>C≡C(CH<sub>2</sub>)<sub>t</sub>H, or C<sub>3-7</sub> cycloalkyl;

$p$  is 1, 2, or 3;

$t$  is 0 or 1;

W is N or C-R, wherein R is hydrogen, halogen, or cyano;

Q<sub>1</sub> is hydrogen, halogen, C<sub>1-2</sub> haloalkyl, C<sub>1-2</sub> alkyl, C<sub>1-2</sub> alkoxy, or C<sub>1-2</sub> haloalkoxy;

Q<sub>2</sub> is A<sup>1</sup> or A<sup>2</sup>;

Q<sub>3</sub> is A<sup>1</sup> when Q<sub>2</sub> is A<sup>2</sup> and Q<sub>3</sub> is A<sup>2</sup> when Q<sub>2</sub> is A<sup>1</sup>;

wherein

A<sup>1</sup> is hydrogen, halogen, C<sub>1-3</sub> alkyl, C<sub>1-3</sub> haloalkyl, -OR<sup>1</sup>, and

A<sup>2</sup> is the group defined by -(Z)<sub>m</sub>-(Z<sup>1</sup>)-(Z<sup>2</sup>), wherein

Z is CH<sub>2</sub> and m is 0, 1, 2, or 3, or

Z is NR<sup>2</sup> and m is 0 or 1, or

Z is oxygen and m is 0 or 1, or

Z is CH<sub>2</sub>NR<sup>2</sup> and m is 0 or 1;

Z<sup>1</sup> is S(O)<sub>2</sub>, S(O), or C(O); and

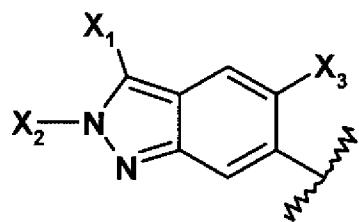
Z<sup>2</sup> is C<sub>1-C4</sub> alkyl, NR<sup>3</sup>R<sup>4</sup>, aryl, arylamino, aralkyl, aralkoxy, or heteraryl;

R<sup>1</sup> is C<sub>1-4</sub> alkyl;

R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are each independently selected from hydrogen, C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl, -S(O)<sub>2</sub>R<sup>5</sup>, and -C(O)R<sup>5</sup>;

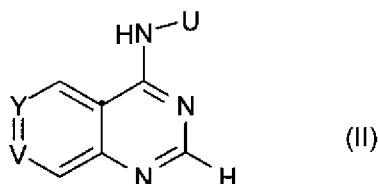
R<sup>5</sup> is C<sub>1-4</sub> alkyl, or C<sub>3-7</sub> cycloalkyl; and

when Z is oxygen then Z<sup>1</sup> is S(O)<sub>2</sub> and when D is



then X<sub>2</sub> is C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C(O)R<sup>1</sup>, or aralkyl; and

(b) a compound of formula II



or a salt, solvate, or physiologically functional derivative thereof;  
wherein

Y is CR<sup>6</sup> and V is N;

or Y is CR<sup>6</sup> and V is CR<sup>7</sup>;

R<sup>6</sup> represents a group CH<sub>3</sub>SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy groups;

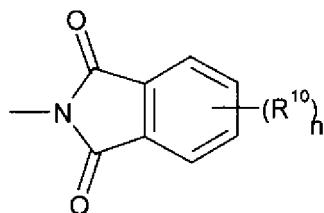
R<sup>7</sup> is selected from the group consisting of hydrogen, halo, hydroxy, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylamino and di[C<sub>1-4</sub> alkyl]amino;

U represents a phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, substituted by an R<sup>8</sup> group and optionally substituted by at least one independently selected R<sup>9</sup> group;

R<sup>8</sup> is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R<sup>8</sup> represents trihalomethylbenzyl or trihalomethylbenzyloxy;

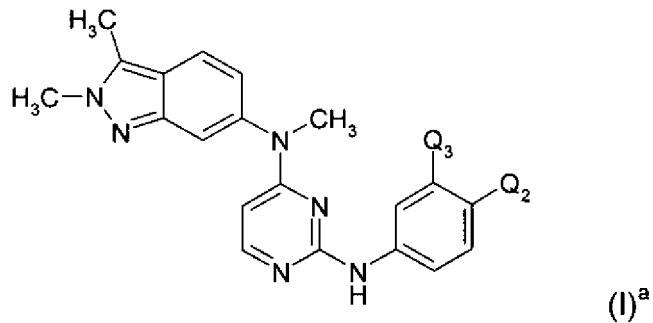
or R<sup>8</sup> represents a group of formula



wherein each R<sup>10</sup> is independently selected from halogen, C<sub>1-4</sub> alkyl and C<sub>1-4</sub> alkoxy; and n is 0 to 3; and

each R<sup>9</sup> is independently hydroxy, halogen, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> alkoxy, amino, C<sub>1-4</sub> alkylamino, di[C<sub>1-4</sub> alkyl]amino, C<sub>1-4</sub> alkylthio, C<sub>1-4</sub> alkylsulphinyl, C<sub>1-4</sub> alkylsulphonyl, C<sub>1-4</sub> alkylcarbonyl, carboxy, carbamoyl, C<sub>1-4</sub> alkoxycarbonyl, C<sub>1-4</sub> alkanoylamino, N-(C<sub>1-4</sub> alkyl)carbamoyl, N,N-di(C<sub>1-4</sub> alkyl)carbamoyl, cyano, nitro and trifluoromethyl.

14. (New) The method of claim 1, wherein (a) the compound of formula I is a compound of formula I<sup>a</sup>



or a salt, solvate or physiologically functional derivative thereof;

wherein Q<sub>3</sub> is A<sup>1</sup> when Q<sub>2</sub> is A<sup>2</sup> and Q<sub>3</sub> is A<sup>2</sup> when Q<sub>2</sub> is A<sup>1</sup>;

wherein

A<sup>1</sup> is hydrogen, halogen, C<sub>1-3</sub> alkyl, and

A<sup>2</sup> is the group defined by -(Z)<sub>m</sub>-(Z<sup>1</sup>)-(Z<sup>2</sup>), wherein

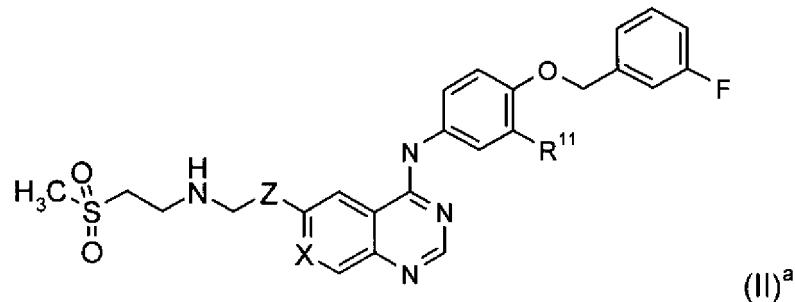
Z is CH<sub>2</sub> and m is 0, 1, 2, or 3;

Z<sup>1</sup> is S(O)<sub>2</sub>, S(O), or C(O); and

Z<sup>2</sup> is C<sub>1-4</sub> alkyl, or NR<sup>3</sup>R<sup>4</sup>;

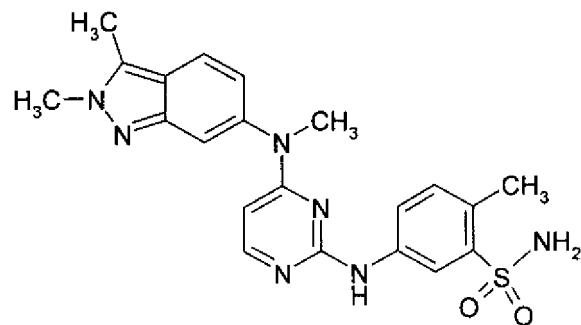
$R^3$  and  $R^4$  are each independently selected from hydrogen, or C<sub>1-4</sub> alkyl; and

(b) the compound of formula II is a compound of formula II<sup>a</sup>



or a salt, solvate or physiologically functional derivative thereof; wherein  $R^{11}$  is –Cl or –Br, X is CH, N, or CF, and Z is thiazole or furan.

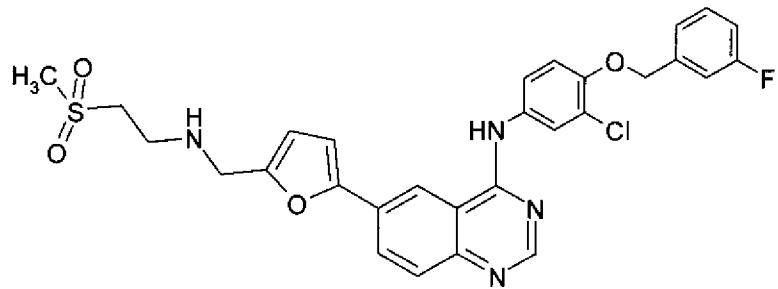
15. (New) The method of claim 1, wherein (a) the compound of formula I is a compound of formula I<sup>b</sup>



(I)<sup>b</sup>

or a salt, solvate, or physiological functional derivative thereof; and

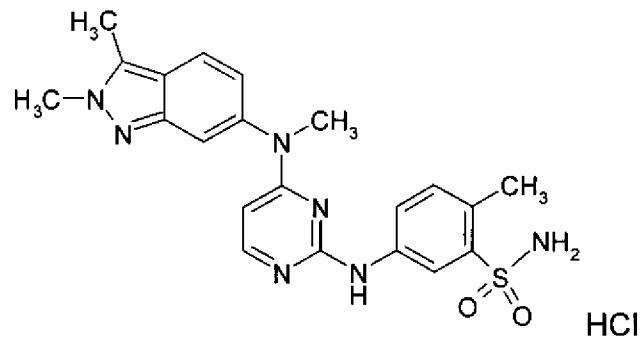
(b) the compound of formula II is a compound of formula II<sup>b</sup>



(II)<sup>b</sup>

or a salt, solvate, or physiological functional derivative thereof.

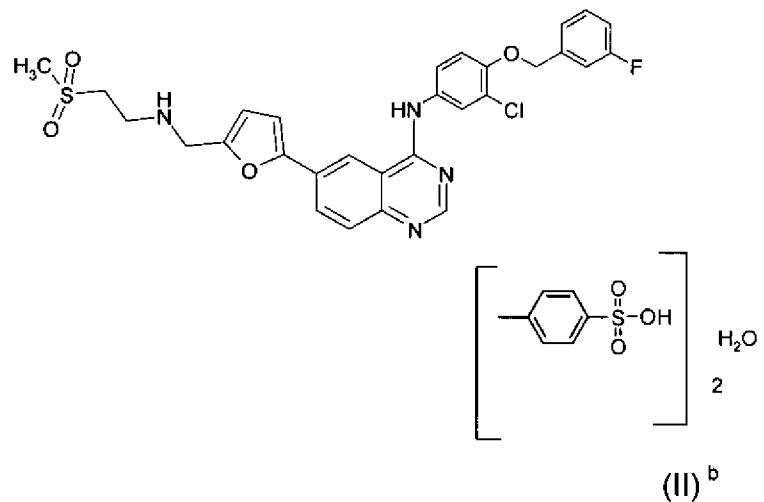
16. (New) The method of claim 1, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I<sup>b</sup>



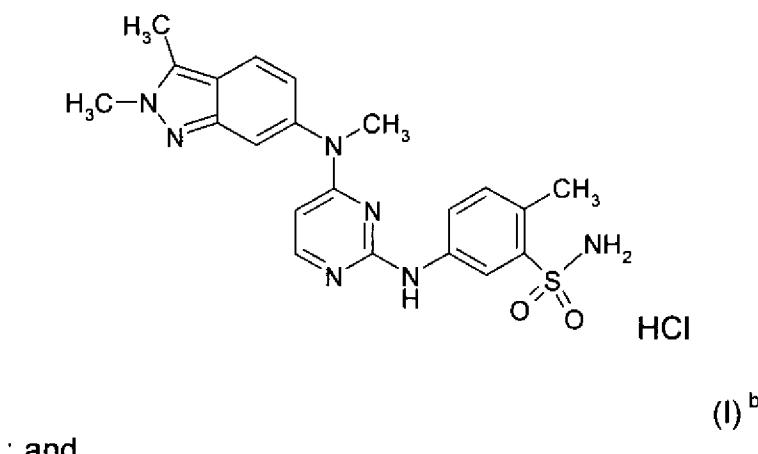
(I)<sup>b</sup>

; and

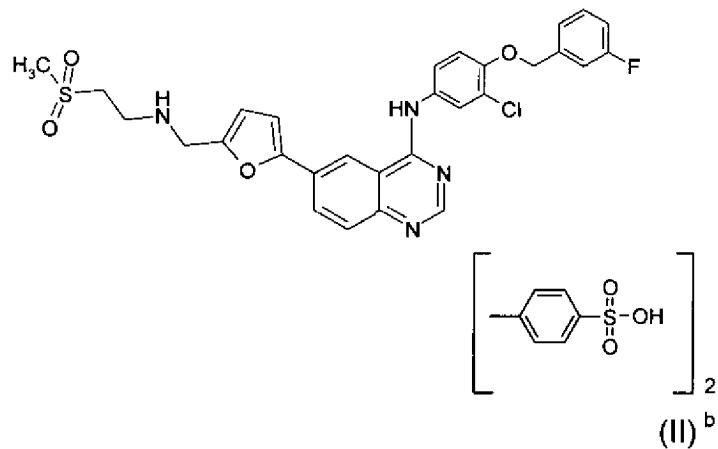
(b) the compound of formula II is a monohydrate ditosylate salt of a compound of formula II<sup>b</sup>



17. (New) The method of claim 1, wherein the compound of formula I is a monohydrochloride salt of a compound of formula I<sup>b</sup>

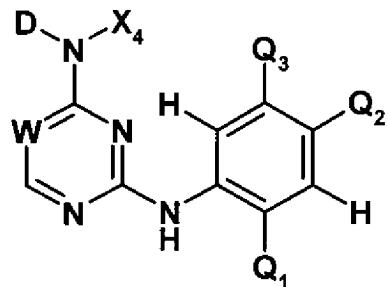


(b) the compound of formula II is an anhydrous ditosylate salt of a compound of formula II<sup>b</sup>



18. (New) A pharmaceutical composition comprising:

(a) a compound of formula I

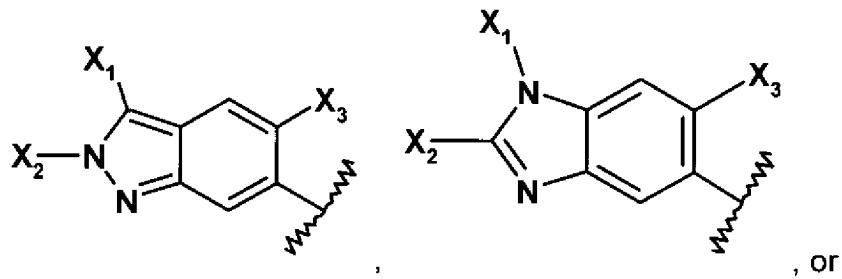


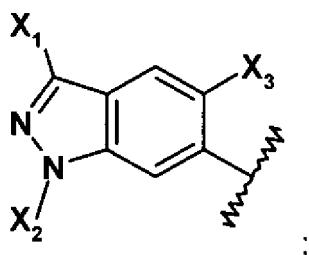
(I)

or a salt, solvate, or physiologically functional derivative thereof;

wherein:

D is





$X_1$  is hydrogen,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, or  $C_{1-4}$  hydroxyalkyl;

$X_2$  is hydrogen,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl,  $C(O)R^1$ , or aralkyl;

$X_3$  is hydrogen or halogen;

$X_4$  is hydrogen,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, heteroaralkyl, cyanoalkyl,  $-(CH_2)_pC=CH(CH_2)_tH$ ,  $-(CH_2)_pC\equiv C(CH_2)_tH$ , or  $C_{3-7}$  cycloalkyl;

$p$  is 1, 2, or 3;

$t$  is 0 or 1;

$W$  is N or C-R, wherein R is hydrogen, halogen, or cyano;

$Q_1$  is hydrogen, halogen,  $C_{1-2}$  haloalkyl,  $C_{1-2}$  alkyl,  $C_{1-2}$  alkoxy, or  $C_{1-2}$  haloalkoxy;

$Q_2$  is  $A^1$  or  $A^2$ ;

$Q_3$  is  $A^1$  when  $Q_2$  is  $A^2$  and  $Q_3$  is  $A^2$  when  $Q_2$  is  $A^1$ ;

wherein

$A^1$  is hydrogen, halogen,  $C_{1-3}$  alkyl,  $C_{1-3}$  haloalkyl,  $-OR^1$ , and

$A^2$  is the group defined by  $-(Z)_m-(Z^1)-(Z^2)$ , wherein

$Z$  is  $CH_2$  and  $m$  is 0, 1, 2, or 3, or

$Z$  is  $NR^2$  and  $m$  is 0 or 1, or

$Z$  is oxygen and  $m$  is 0 or 1, or

$Z$  is  $CH_2NR^2$  and  $m$  is 0 or 1;

$Z^1$  is  $S(O)_2$ ,  $S(O)$ , or  $C(O)$ ; and

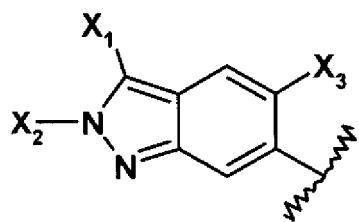
$Z^2$  is  $C_{1-4}$  alkyl,  $NR^3R^4$ , aryl, arylamino, aralkyl, aralkoxy, or heteroaryl;

$R^1$  is  $C_{1-4}$  alkyl;

$R^2$ ,  $R^3$ , and  $R^4$  are each independently selected from hydrogen,  $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl,  $-S(O)_2R^5$ , and  $-C(O)R^5$ ;

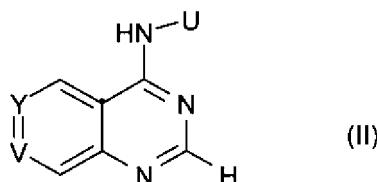
$R^5$  is  $C_{1-4}$  alkyl, or  $C_{3-7}$  cycloalkyl; and

when Z is oxygen then Z<sup>1</sup> is S(O)<sub>2</sub> and when D is



then X<sub>2</sub> is C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C(O)R<sup>1</sup>, or aralkyl; and

(b) a compound of formula II



or a salt, solvate, or physiologically functional derivative thereof;

wherein

Y is CR<sup>6</sup> and V is N;

or Y is CR<sup>6</sup> and V is CR<sup>7</sup>;

R<sup>6</sup> represents a group CH<sub>3</sub>SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy groups;

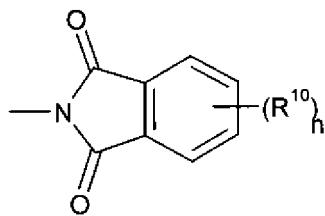
R<sup>7</sup> is selected from the group consisting of hydrogen, halo, hydroxy, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylamino and di[C<sub>1-4</sub> alkyl]amino;

U represents a phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, substituted by an R<sup>8</sup> group and optionally substituted by at least one independently selected R<sup>9</sup> group;

R<sup>8</sup> is selected from the group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl;

or R<sup>8</sup> represents trihalomethylbenzyl or trihalomethylbenzyloxy;

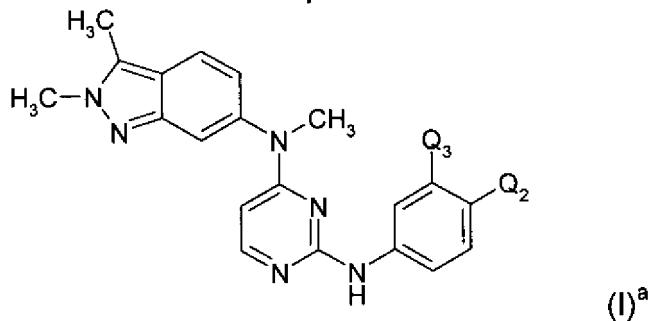
or R<sup>8</sup> represents a group of formula



wherein each  $R^{10}$  is independently selected from halogen, C<sub>1-4</sub> alkyl and C<sub>1-4</sub> alkoxy; and n is 0 to 3; and

each  $R^9$  is independently hydroxy, halogen, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> alkoxy, amino, C<sub>1-4</sub> alkylamino, di[C<sub>1-4</sub> alkyl]amino, C<sub>1-4</sub> alkylthio, C<sub>1-4</sub> alkylsulphinyl, C<sub>1-4</sub> alkylsulphonyl, C<sub>1-4</sub> alkylcarbonyl, carboxy, carbamoyl, C<sub>1-4</sub> alkoxy carbonyl, C<sub>1-4</sub> alkanoylamino, N-(C<sub>1-4</sub> alkyl)carbamoyl, N,N-di(C<sub>1-4</sub> alkyl)carbamoyl, cyano, nitro and trifluoromethyl.

19. (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a compound of formula I<sup>a</sup>



or a salt, solvate or physiologically functional derivative thereof;

wherein  $Q_3$  is A<sup>1</sup> when  $Q_2$  is A<sup>2</sup> and  $Q_3$  is A<sup>2</sup> when  $Q_2$  is A<sup>1</sup>;

wherein

A<sup>1</sup> is hydrogen, halogen, C<sub>1-3</sub> alkyl, and

A<sup>2</sup> is the group defined by -(Z)<sub>m</sub>-(Z<sup>1</sup>)-(Z<sup>2</sup>), wherein

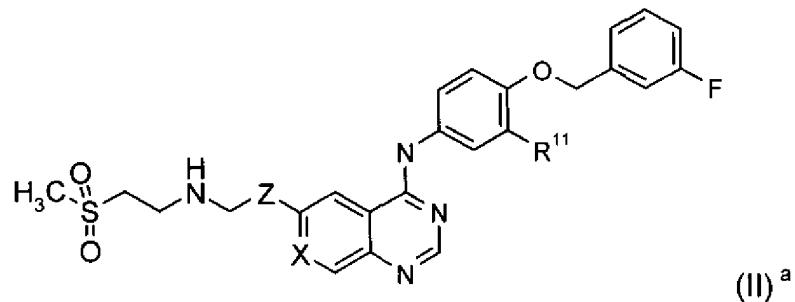
Z is CH<sub>2</sub> and m is 0, 1, 2, or 3;

Z<sup>1</sup> is S(O)<sub>2</sub>, S(0), or C(O); and

Z<sup>2</sup> is C<sub>1-4</sub> alkyl, or NR<sup>3</sup>R<sup>4</sup>;

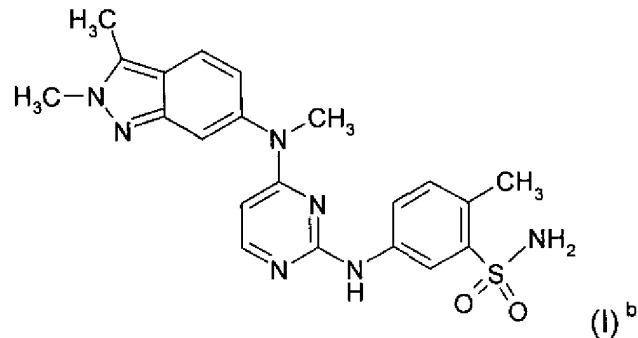
R<sup>3</sup> and R<sup>4</sup> are each independently selected from hydrogen, or C<sub>1-4</sub> alkyl; and

(b) the compound of formula II is a compound of formula II<sup>a</sup>

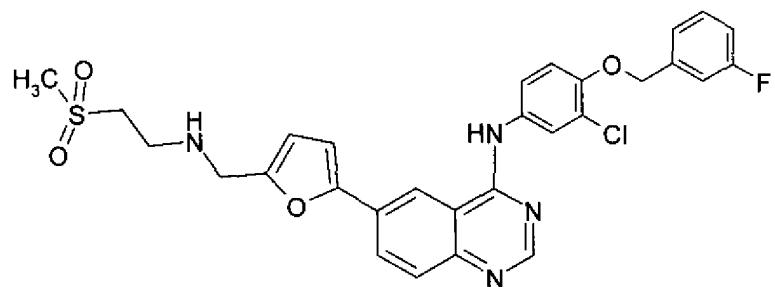


or a salt, solvate or physiologically functional derivative thereof; wherein R<sup>11</sup> is –Cl or –Br, X is CH<sub>2</sub>, N, or CF<sub>3</sub>, and Z is thiazole or furan.

20. (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a compound of formula I<sup>b</sup>



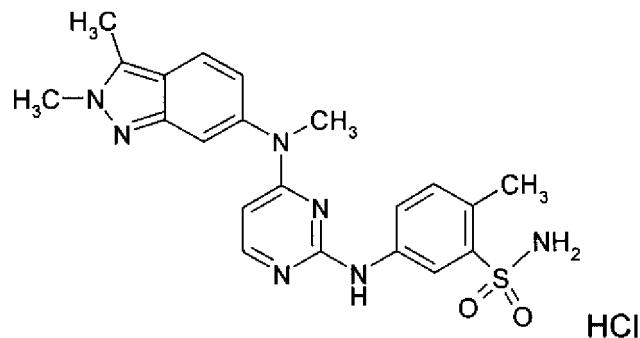
or a salt, solvate, or physiological functional derivative thereof; and  
 (b) the compound of formula II is a compound of formula II<sup>b</sup>



(II)<sup>b</sup>

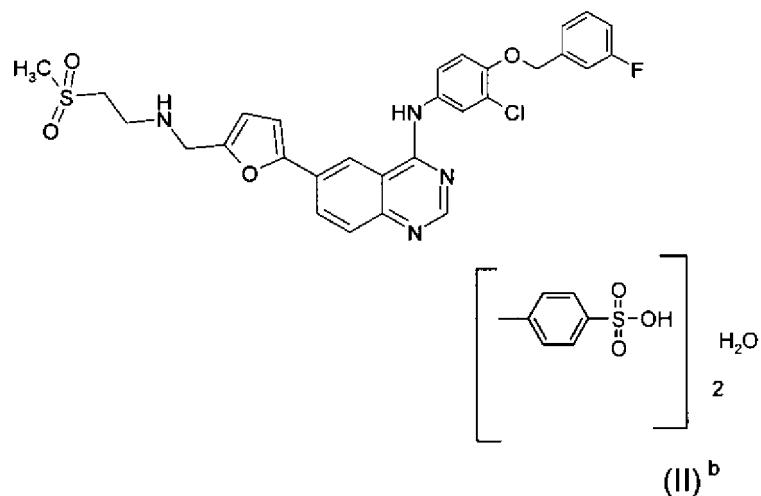
or a salt, solvate, or physiological functional derivative thereof.

21. (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I<sup>b</sup>

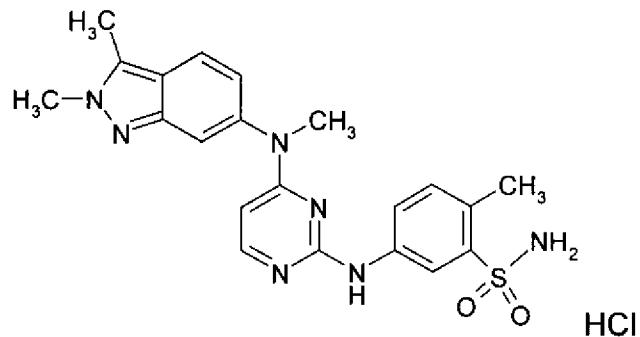
(I)<sup>b</sup>

; and

- (b) the compound of formula II is a monohydrate ditosylate salt of the compound of formula II<sup>b</sup>

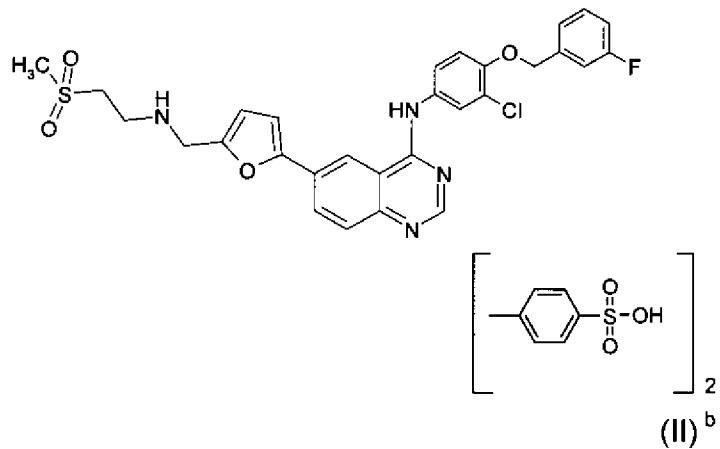
(II)<sup>b</sup>

22. (New) The pharmaceutical composition of claim 6, wherein (a) the compound of formula I is a monohydrochloride salt of a compound of formula I<sup>b</sup>

(I)<sup>b</sup>

; and

- (b) the compound of formula II is an anhydrous ditosylate salt of the compound of formula II<sup>b</sup>



23. (New) A pharmaceutical combination comprising: a compound of formula I, I<sup>a</sup> or I<sup>b</sup> or salt, solvate or physiologically functional derivative thereof, and a compound of formula II, II<sup>a</sup> or II<sup>b</sup> or salt, solvate or physiologically functional derivative thereof for use in therapy.

24. (New) The use of a pharmaceutical combination comprising: a compound of formula I, I<sup>a</sup> or I<sup>b</sup> or salt, solvate or physiologically functional derivative thereof, and a compound of formula II, II<sup>a</sup> or II<sup>b</sup> or salt, solvate or physiologically functional derivative thereof for the preparation of a medicament useful in the treatment of cancer.